

REMARKS

Claims 14 and 20 are pending. Claims 15 and 31 have been canceled without prejudice or disclaimer and solely for the purpose of expediting prosecution. Claims 3-6, 8-9, 12-13, 16-19, 21-22, 24-25, and 27-28 were previously canceled. Claims 1-2, 7, 10-11, 23, 26, and 29-30 are withdrawn. Claims 14 and 20 have been amended to recite that the isolated recombinant megakaryocyte tyrosine kinase 1, or fusion protein thereof, has the amino acid sequence of SEQ ID NO. 2. Support for this amendment is found throughout the specification; see, for instance, the legend for Figure 9 at page 9 of the specification and the third and fourth paragraphs of page 13.

II. Applicants overcome the Examiner's rejections

1. The Examiner states that "[T]he title of the invention is not descriptive." Office Action at page 2. Applicants have amended the title to reflect that the claimed invention is directed to a "Novel Megakaryocytic Protein Tyrosine ~~Kinases~~ Kinase 1."

2. The Examiner states that "[T]he abstract of the disclosure is objected to because the abstract is in two paragraphs." Office Action at page 2. Accordingly, Applicants have combined the two paragraphs into one and have appended a clean copy of the abstract, on a separate sheet, to this paper.

3. Applicants have amended page 1 of the specification to relate the lineage of the present application, *i.e.*, that it is a divisional application of U.S. application serial no. 08/232,545, filed on April 22, 1994, now U.S. patent No. 6,506,578. Applicants also have submitted an Application Data Sheet conveying this lineage.

4. The Examiner rejected claims 14, 15, 20, and 31 under 35 U.S.C. § 112, second paragraph for (a) reciting "an isolated recombinant MKK1" in claim 14; (b) reciting Figures 1A, 1B, and 1C for the sequence of MKK1 in claim 15; and (c) for reciting "MKK1 protein." Office Action at page 3.

Applicants have amended the claims to recite a "megakaryocyte tyrosine kinase 1" and to specify that the megakaryocyte tyrosine kinase 1 protein has the amino acid sequence

of SEQ ID NO. 2. For these reasons, Applicants respectfully request that the Examiner withdraw these rejections.

5. The Examiner rejected claims 14 and 20 under 35 U.S.C. § 112, first paragraph as lacking written description, because “the specification does not disclose all the MKK1 polypeptides.” Office Action at page 4.

Applicants have amended claims 14 and 20 to recite that a megakaryocyte tyrosine kinase 1 protein has the amino acid sequence of SEQ ID NO. 2, for which there is sufficient written description support. The Examiner acknowledges that “the specification discloses MKK1 polypeptide of SEQ ID NO. 2. This meets the written description and enablement provisions of 35 U.S.C. § 112, first paragraph” (emphasis added; Office Action at page 4). Accordingly, Applicants submit that there is written description for the presently claimed invention and respectfully request that the Examiner withdraw this rejection.

6. The Examiner rejected claims 14 and 20 under 35 U.S.C. § 112, first paragraph as lacking enablement because “the lack of description of the various MKK1 forms in the specification does not enable one of skilled in the art [to] make and/or use the invention.” Office Action at page 6.

Applicants’ amendment overcomes the rejection for the reasons cited in the previous subsection, which also is in keeping with the Examiner’s acknowledgement that an MKK1 of SEQ ID NO. 2 is enabled. See page 7 of the Office Action. Accordingly, Applicants submit that the presently claimed invention is enabled and respectfully requests that the Examiner withdraw this rejection.

7. Claims 14 and 15 are rejected under 35 U.S.C. § 102(a) as being allegedly anticipated by Bennett *et al.*, *J. Biol. Chem.*, 269(2), pp. 1068-74, January 14, 1994, or Sakano *et al.*, *Oncogene*, 9(4), pp. 1155-61, April, 1994. Office Action at pages 8 and 9.

Applicants have filed herewith a declaration executed by Ricardo Martinez, a research scientist who was employed at Sugen, which is a collaborator of the assignee of the present application (Max-Planck). Dr. Martinez attests that he sequenced the claimed megakaryocyte

tyrosine kinase 1 before the publication date of Bennett *et al.* Since the declaration antedates both of the cited references, neither is available as prior art against the present claims. Accordingly, none of the claims are anticipated and, thus, this rejection is moot.

8. Claims 20 and 31 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Bennett *et al.*, *supra*, or Sakano *et al.*, *supra*, in view of Maniatis *et al.*, 1982, pages 422-430. Office Action at page 9.

For the reasons cited in the preceding subsection, Ricardo Martinez's declaration evidences Applicants' isolation and identification of the DNA and amino acid sequences of megakaryocyte tyrosine kinase 1 prior to Bennett *et al.* and Sakano *et al.* Accordingly, neither may be combined with the referenced Maniatis publication. Therefore, none of the claims are rendered obvious and, thus, this rejection is moot.

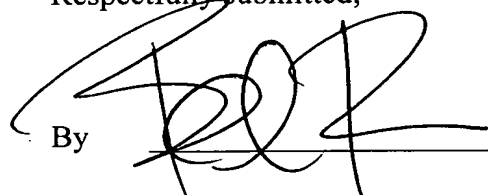
III. Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Date March 2, 2004

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5475
Facsimile: (202) 672-5399

Respectfully submitted,

By 
Beth A. Burrous
Attorney for Applicant
Registration No. 35,087

PROJECT _____

Map Draw India of ORF

Page 1

MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

Enzymes: All 335 enzymes (No Filter)

Settings: Linear, Certain Sites Only, Standard Genetic Code

GTGCAGCGGGACGCTCGGGTGTGCAGCCGCTCGCGGAGGCCCTCTGGGGGGGGSGCSCGGGCGCGGCT 70

CACGTGCGCCTGCGAGCCACACGTGCGCCGAGCGCTCCGGAGGACCCCCCCCCSCGSGCCCGCGCCGA

Only once

Below

SUG#301

SUG#313

V O R D A R V C S R L A E A S W G G ? ? G R G
 C S G T L G C A A G S R R P P G G G ? ? G A A
 C A A G R S G V O P A R G G L L G G G A R A R L

CGGGGCGCCCCYTRAGCAGAAAACAGGRAGAACCAGGCTSGGTCHAGTGGCACCMAGCTCCCTACYTCY 140
 GCCCCGCGGGGRAYTCGTCTTTTGTCCYTCTTGGTCCGASCCAGKTCACCGTGGKTCGAGGGATGRAGR

Below

SUG#301

SUG#313

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 R G R P L S R K Q ? E P G ? V ? W H ? A P Y ?
 G G A P . A E N R ? N Q A ? S S G T ? L P T S

KGTGCMAGCCGCTKGCTGTGGCAGGCCAWTCCCARCGKYCCGACTGTGACCACTTGCTCAGTGTGCC 210
 MCACGKTCGGCGGAMCGGACACCGTCCGGTWAGGGTYGCMRGGGCTGACACTGGTGAACGAGTCACACGG

Below

SUG#301

SUG#313

V ? A A ? P V A G ? S Q R ? R L . P L A Q C A
 ? C ? P P ? L W Q A ? P ? ? P D C D H L L S V P
 ? A S R L A C G R P ? P ? ? P T V T T C S V C

Read and Understood By

R. M. M.
 Signed

Date

[Signature]
 Signed

Date

0 0 1 2 9 6

PROJECT

MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

TCTCACSDGYCYCAKTTTCCCTCTGKGGGGCGATAGCGSGGCGAGGCTCTCTGGTTTCCTGGCGGGCAT 280
 AGAGTGSHERGRGTNAAAGGGAGACMCCCCGCTATCCGSCCGCTCCGAGAGACCAAAGGACCGCCCGTA

Below

SUG#301

SUG#313

SUG#304

SUG#304

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 L T ? ? ? F P L ? G D R R G E A L W F P G G H
 L S ? ? ? ? S L ? G A I G ? A R L S G F L A G I

TTCACGGCTGTGATTCTGCTGAGGAACCTCCCCGGGTGAGCCCCGCTTCTCCGAGCCTGGCACCCCCC 350
 AAGTGCCGACACTAAGACGACTCCTTGAAGGGGCCACTCGGGGGCGAAGGAGGCTCGGACCGTGGGGGG

One strand

SUG#313

SUG#313

SUG#304

SUG#304

F H G C D S A E E L P R V S P R F L R A W H P P
 F T A V I L L R N F P G . A P A S S E P G T P
 S R L . F C . G T S P G E P P L P P S L A P P

TCCCGTCTCAGCCAGGATGCCAACGAGGCGCTGGCCCCGGGACCCAGTGTATCACCAAATGCGAGCAC 420
 AGGGCAGAGTCGGTCTACGGTTGCTCCGCGACCCGGGGCCCGTGGGTACATAGTGGTTTACGCTCGTG

One strand

SUG#313

SUG#313

SUG#304

SUG#304

SUG#301

P V S A R N P T R R W A P G T O C I T K C E H
 L P S O P G C O R G A G P R A P S V S P N A S T
 S R L S O D A N E A L G P G H P V Y H O M R A

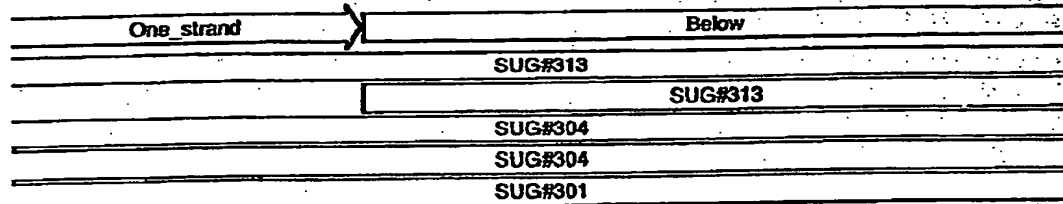
RR Mr

light. phle renders slow identical renders But in human
 Gyl. (P.2)

M. J. J.

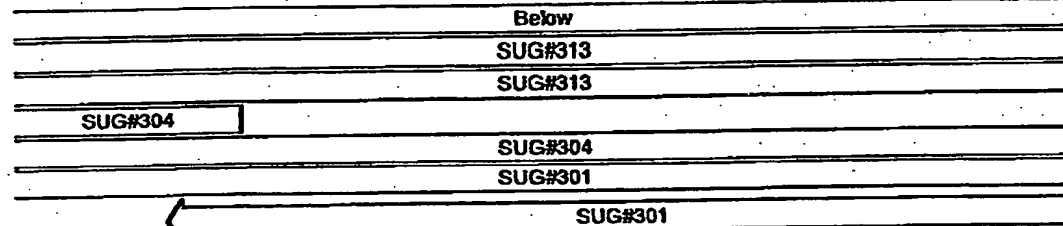
MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

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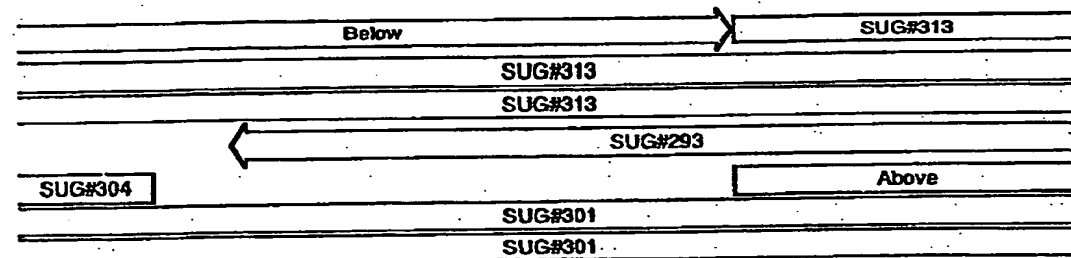
T R P K P G E L A F R K G D V V T I L E A C E
P A P S Q G S W P S A R A T W S P S W R P A R
H P P Q A R G A G L P Q G R R G H H P G G L R E

ACAAGAGCTGGTACCGCGTCAAGCACCAACAGTGGACAGGAGGGGCTGCTGGCAGCTGGGGCGCTGCG 560
TGTTCTCGACCATGGCGCAGTTCGTGGTGTGGTCACTGTCTCCCGACGACCGTGGACCCCGGACGC



N K S W Y R V K H H T S G Q E G L L A A G A L R
T R A G T A S S T T P V D R R G C W O L G R C
Q E L V P R Q A P H O W T G G A A G S W G A

GGAGCGGGAGGCCCTCTCCGACAGCCCCAAGCTCAGCCTCATGCCGTGGTTCACGGGAAGATCTCGGGC 630
CCTCGCCCTCCGGGAGAGGCGTCTGGGGTTCGAGTCGGAGTACGGCACCAAGGTGCCCTTCTAGAGCCCG



E R E A L S A D P K L S L H P W F H G K I S G
G S G R P S P O T P S S A S C R G S T G R S R A

Signed

Date

Signed

Date

001297

MKK1-3, consensus 4/12 Map (1 > 2053) Site and Sequence

G G G P L R R P O A O P H A V V P R E D L G

CAGGAGGCTGTCCAGCAGCTGCAGCCTCCCGAGGATGGCTGTTCTTGGTGGGGAGTCCGCGCGCCACC 700
GTCCTCCGACAGGTCGTGACGTGGAGGGCTCTACCCGACAAGGACCACGCCCTCAGGCGCGCGGTGG

SUG#313

SUG#313

SUG#313

SUG#293

Above

SUG#301

SUG#301

SUG#313

SUG#293

O E A V O O L O P P E D G L F L V R E S A R H
R R L S S S C S L P R M G C S W C G S P R A T
P G G C P A A A S R G W A V P G A G V R A P PCCGGCGACTACGTCTGTGCGTGAGCTTTGGCCGCGACGTATCCACTACCGCTGCTGCACCGCGACGG 770
GGCCGCTGATGCAGGACACGCACTCGAAACCGCGCTGCAGTAGGTGATGGCGCACGACGTGGCGCTGCC

SUG#313

SUG#313

SUG#313

SUG#313

SUG#293

Above

SUG#301

SUG#313

SUG#293

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P A T T S C A A L A A T S S T T A C C T A T
R R L R P V R E L W P R R H P L P R A A P R R

KR m (Signed)

L/M/C

MR. S

MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

CCACCTCACAATCGATGAGGCCGTCTTCTTCTGCAACCTCATGGACATGGTGGAGCATTACAGCAAGGAC
GGTGGAGTGTTAGCTACTCCGGCACAAGAAGACGTTGGAGTACCTGTACCACCTCGTAATGTCGTTCTCTG

840

SUG#313

SUG#313

SUG#313

SUG#293

Above

SUG#313

SUG#313

SUG#293

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A T S O S M R P C S S A T S W T W W S I T A R T
P P H N R G R V L L O P H G H G G A L O O G

AAGGGCGCTATCTGCACCAAGCTGGTGAGACCAAAGCGGAAACACGGGACCAAGTCGGCCGAGGAGGAGC
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910

SUG#313

SUG#313

SUG#313

SUG#293

Above

SUG#313

SUG#313

SUG#293

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R A L S A P S W D O S G N T G P S R P R R S
O G R Y L H O A G E T K A E T R D O V G R G G A

TGGCCAGGGCGGGCTGGTTACTGAACCTGCAGCATTGACATTGGGAGCACAGATCGGAGAGGGAGAGTT
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980

SUG#313

SUG#313

SUG#313

SUG#282

SUG#293

Above

SUG#313

SUG#282

SUG#313

R 52 MS

M 12 MS

MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

SUG#293

L A R A G W L L N L O H L T L G A Q I G E G E F
W P G R A G Y T C S I H W E H R S E R E S
G O G G L V T E P A A F D I G S T D R R G R V

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SUG#313

SUG#313

SUG#282

SUG#293

Above

SUG#313

SUG#282

SUG#313

SUG#293

SUG#301

(Purified not after)
G ? ? L O G E Y L G O K V A V K N I K C D V T
L E L ? C R V S T W G K R W P R I S S V H ? O
W S C P A G V P G A K G G R E E Y O V C ?

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CGGGTCCGGAAGGACCTGCTCTGCCGGCAGTACTGCTTCTACGTTGTGCTCTTGGACCACGCAGAGGACC

1120

SUG#313

SUG#313

SUG#282

SUG#293

SUG#304

Above

SUG#313

SUG#282

SUG#313

5'end

SUG#301

A O A F L D E T A V H T K H O H E N L V R L L
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S P G L P G R D G R H D E D A T R E P G A S P G

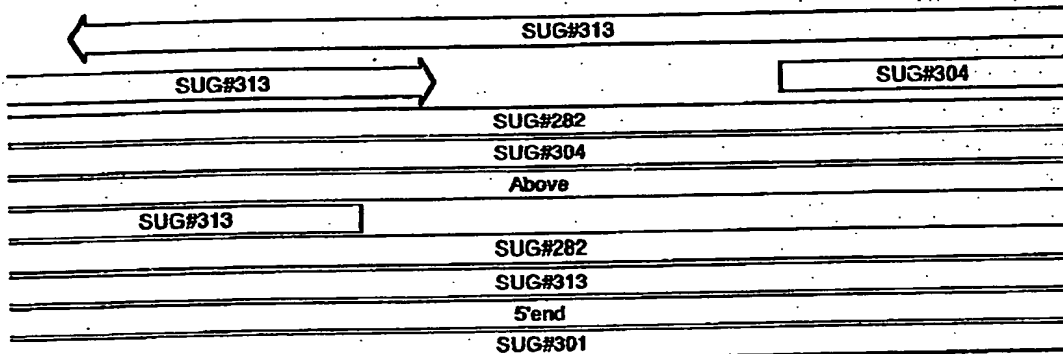
R2 Mh

AP 47

MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

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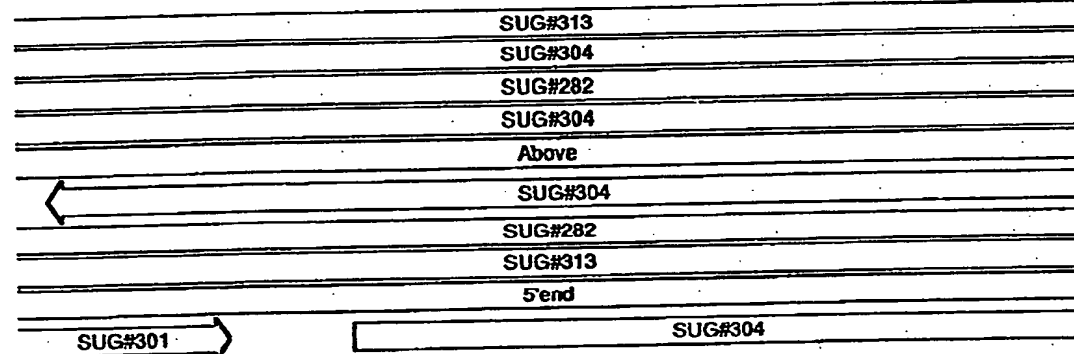
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G V I L H O G L Y I V M E H V S K G N L V N F L
A S C T R G C T L S W S T A R A T W T F
R D P A P G A V H C H G A R E Q G Q P G E L S

GGCGACCCGGGGTCGAGCCCTCGTGAACACCGCTCAGCTCCTGCAGTTTTCTCTGCACGTGGCCGAGGGC
CGCCTGGGCCCCAGCTCGGGAGCACTTGTGGCGAGTCGAGGACGTCAAAGAGACGTGCACCGGCTCCCG

1260



R T R G R A L V N T A Q L L O F S L H V A E G
C G P G V E P S T P L S S C S F L C T W P R A
A D P G S S P R E H R S A P A V F S A R G R G

RZ mtr
Signed

Date

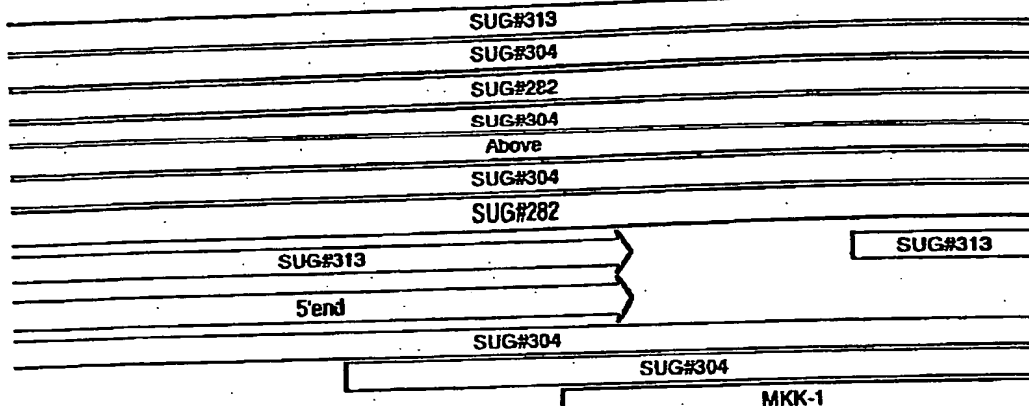
mport
Signed

Date

001299

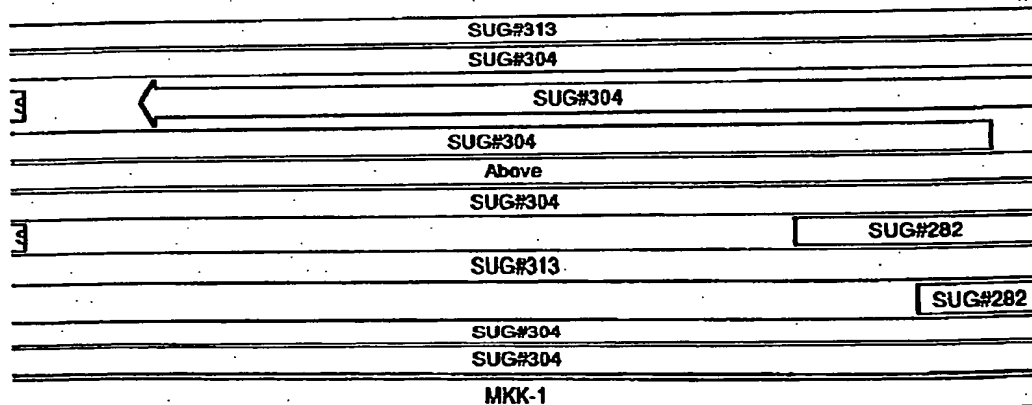
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H E Y L E S K K L V H R D L A A R N I L V S E
W S T W R A R S L C T A T W P P A T S W S O R
H G V P G E O E A C A P R P G R P O H P G L R G

ACCTGGTGGCCAAGGTCAGCGACTTTGGCCTGGCCAAAGCCGAGCGGAAGGGGCTAGACTCAAGCCGGCT 1400
TGGACCACCGGTTCCAGTCGCTGAAACCGGACCGGTTTCGGCTCGCCTTCCCCGATCTGAGTTCGGCCGA



D L V A K V S D F G L A K A E R K G L D S S R L
T W W P R S A T L A W P K P S G R G . T Q A G
P G G O G O R L W P G O S R A E G A R L K P A

R. R. M. T.
Signed

Date

M. R. T.
Signed

Date

MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

G C C C G T C A A G T G G A C G G C G C C C G A G G C T C T C A A A C A C G G G A A G T T C A C C A G C A A G T C G G A T G T C T G G A G T

C G G G C A G T T C A C C T G C C G C G G G C T C C G A G A G T T T G T G C C C T T C A A G T G G T C G T T C A G C C T A C A G A C C T C A

1470

Below

SUG#304

SUG#304

Above

SUG#304

SUG#282

SUG#313

SUG#282

SUG#304

SUG#304

MKK-1

P V K W T A P E A L K H G K F T S K S D V W S
C P S S G R R P R L S N T G S S P A S R M S G V
A R Q V D G A R G S O T R E V H Q Q V G C L E

T T T G G G T G C T G C T C T G G G A G G T C T T C T C A T A T G G A C G G G C T C C G T A C C C T A A A A T G T C A C T G A A A G A G G

A A A C C C C A C G A C G A G A C C C T C C A G A A G A G T A T A C C T G C C C G A G G C A T G G G A T T T T A C A G T G A C T T T C T C C

1540

Below

SUG#304

SUG#304

SUG#282

SUG#313

SUG#282

SUG#304

F G V L L W E V F S Y G R A P Y P K M S L K E
L G C C S G R S S H M D G L R T L K C H K R
F W G A A L G G L L I W T G S V P N V T E R G

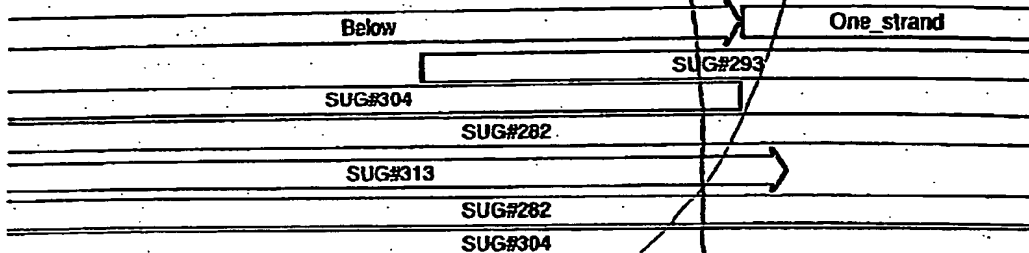
RR hr
signed

mf
signed

Possible ORF change
 Terminator to left of (P) 3000 later (see P. 23)

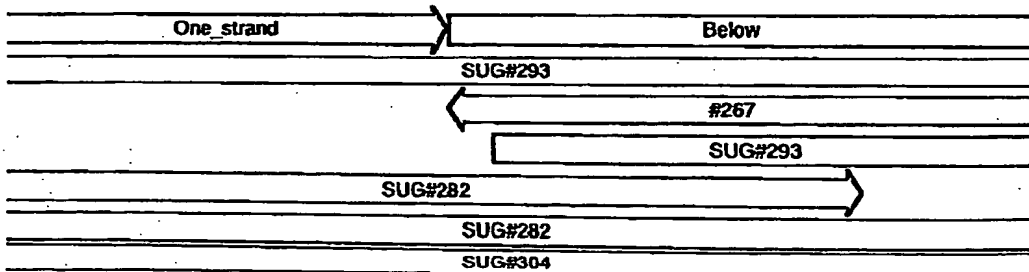
MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

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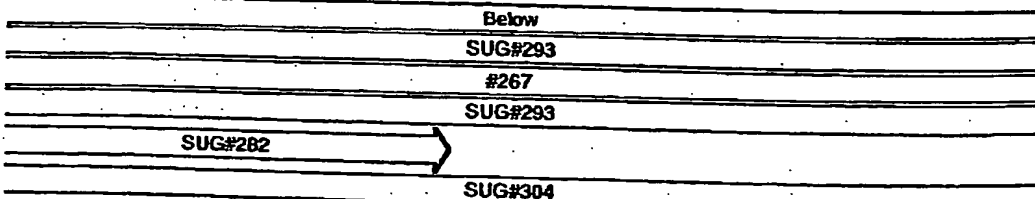
V S E A L E K G Y R H E P P R G S R P V H V L
 C R R P W R R G T A W N P P E G C P G P C T Y
 V G G P G E G V P H G T P P R A V O A R A R T

CATGAGCAGCTGCTGGGAGGCAGAGCCCGCCGCCACCCTTCCGCAAACTGGCCGAGAAGCTGGCCCC 1680
 GTACTCGTCGACGACCCCTCCGTCTCGGGGGGGCGCCGGTGGGAAGGCGTTTGACCGGCTCTTCGACCGGG



H S S C W E A E P A A G H P S A N W P R S W P
 S A A A G R O S P P P A T L P O T G R E A G P
 H E O L L G G R A R R R P P F R K L A E K L A

GGGAGCTACGCAGTGCAGGTGCCCCAGCCTCCGTTCTCAGGGCAGGACGCCGACGGCTCCACCTCGCCCC 1750
 CCCTCGATGCGTCACGTCCACGGGGTGGAGGCAAGAGTCCCGTCTGCGGCTGCCGAGGTGGAGCGGGG



G S Y A V O V P Q P P F S G O D A D G S T S P
 G A T O C R C P S L R S G R T P T A P P R P

Rem

MR

MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

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GAAGCCAGGAGCCCTGACCCCAACCGGTGGGGCCCTTGGCCAGAGGACCGAGAGAGTGGAGAGTACGGC 1820
CTTCGGTCCTCGGGACTGGGGTGGGCCACCCCGGAACCGGTCTCTGGCTCTCTCACCTCTCATGCCG

Below

SUG#293

#267

SUG#293

SUG#304

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E A R S P D P T R W G P W P R G P R E W R V R
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CACCCCGTGACTGGTCCGGGTCTCTCCAGGTCCGCCGTTAGTAGGAGGACCACGGGTGTCGTCCCC

Below

SUG#293

#267

SUG#293

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R G G T D O A O G G S R R A S H P P G A H S R G
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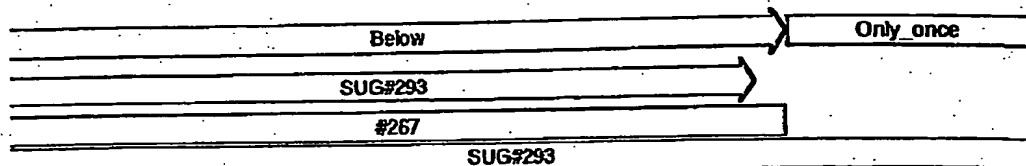
SUG#293

L A H V G G S G R P V D T P D L R R M I A R
W P T G A L G G P W T P O T C E G S P D K
A G P R R G L W A A R G H P R P A K D D R P I KRz Mr
Signedmef
Date

001301

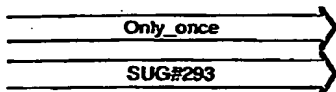
MKK1-3 consensus 4/12 Map (1-2053) Site and Sequence

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R R I L R T L K K G G A R Y P I R P I V S R I K
 D G F . G L . K K G G P G T O F A L . V V L
 T D S K D S K K R G G P V P N S P Y S E S Y

AATTAAGTGGCCGTCGTTTAAAT 2053
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I N W P S F
 K L T G R R F N
 N . L A V V L M

PR [redacted]

mf [redacted]